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<110> CALIFORNIA INSTITUTE OF TECHNOLOGY
LYAPINA, Svetlana
VERMA, Rati
DESHAIES, Raymond
<120> REGULATION OF TARGET PROTEIN ACTIVITY THROUGH MODIFIER PROTEINS
<130> CIT1510-3
<150> US 60/261,314
<151> 2001-01-12
<150> US 60/322,322
<151> 2001-09-14
<150> US 60/322,030
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<160> 22
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Leu Asp Arg Lys Leu Leu Glu Leu Leu Trp Asn Lys Tyr Trp Val Asn

Thr Leu Ser Ser Ser Leu Leu Thr Asn Ala Asp Tyr Thr Thr Gly 165 170 175

Gln Val Phe Asp Leu Ser Glu Lys Leu Glu Gln Ser Glu Ala Gln Leu 180 185 190

Gly Arg Gly Ser Phe Met Leu Gly Leu Glu Thr His Asp Arg Lys Ser 195 200 205

Glu Asp Lys Leu Ala Lys Ala Thr Arg Asp Ser Cys Lys Thr Thr Ile 210 215 220

Glu Ala Ile His Gly Leu Met Ser Gln Val Ile Lys Asp Lys Leu Phe 225 230 235 240

Asn Gln Ile Asn Ile Ser 245

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Val Ser Val Glu Ala Val Asp Pro Val Phe Gln Ala Lys Met Leu Asp 20 25 30

Met Leu Lys Gln Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His 35 40 45

Ser His Pro Gly Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr 50 55 60

Gln Gln Ser Phe Glu Ala Leu Ser Glu Arg Ala Val Ala Val Val 65 70 75 80

Asp Pro Ile Gln Ser Val Lys Gly Lys Val Val Ile Asp Ala Phe Arg 85 90 95

Leu Ile Asn Ala Asn Met Met Val Leu Gly His Glu Pro Arg Gln Thr
100 105 110

Thr Ser Asn Leu Gly His Leu Asn Lys Pro Ser Ile Gln Ala Leu Ile 115 120 125 His Gly Leu Asn Arg His Tyr Tyr Ser Ile Thr Ile Asn Tyr Arg Lys 130 135

Asn Glu Leu Glu Gln Lys Met Leu Leu Asn Leu His Lys Lys Ser Trp 150 155

Met Glu Gly Leu Thr Leu Gln Asp Tyr Ser Glu His Cys Lys His Asn 170

Glu Ser Val Val Lys Glu Met Leu Glu Leu Ala Lys Asn Tyr Asn Lys 180 185

Ala Val Glu Glu Glu Asp Lys Met Thr Pro Glu Gln Leu Ala Ile Lys 195 200

Asn Val Gly Lys Gln Asp Pro Lys Arg His Leu Glu Glu His Val Asp 210 215

Val Leu Met Thr Ser Asn Ile Val Gln Cys Leu Ala Ala Met Leu Asp 225 235 230

Thr Val Val Phe Lys 245

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<213> Homo sapiens

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Ala Leu Ser Lys Leu Gly Cys Asn Ile Thr Ile Ser Glu Asp Ile Thr

Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Met Glu Arg Met Ala Ser 40

Val Tyr Leu Glu Glu Gly Asn Leu Glu Asn Ala Phe Val Leu Tyr Asn

Lys Phe Ile Thr Leu Phe Val Glu Lys Leu Pro Asn His Arg Asp Tyr 70 75

Gln Gln Cys Ala Val Pro Glu Lys Gln Asp Ile Met Lys Lys Leu Lys 85 90 95

Glu Ile Ala Phe Pro Arg Thr Asp Glu Leu Lys Asn Asp Leu Lys
100 105 110

Lys Tyr Asn Val Glu Tyr Gln Glu Tyr Leu Gln Ser Lys Asn Lys Tyr 115 120 125

Lys Ala Glu Ile Leu Lys Lys Leu Glu His Gln Arg Leu Ile Glu Ala 130 135 140

Gln Phe Leu Phe Phe Glu Asp Gln Leu Lys Lys Gln Glu Leu Ala Arg 165 170 175

Gly Gln Met Arg Ser Gln Gln Thr Ser Gly Leu Ser Glu Gln Ile Asp 180 185 190

Gly Ser Ala Leu Ser Cys Phe Ser Thr His Gln Asn Asn Ser Leu Leu 195 200 205

Asn Val Phe Ala Asp Gln Pro Asn Lys Ser Asp Ala Thr Asn Tyr Ala 210 215 220

Ser His Ser Pro Pro Val Asn Arg Ala Leu Thr Pro Ala Ala Thr Leu 225 230 235 240

Ser Ala Val Gln Asn Leu Val Val Glu Gly Leu Arg Cys Val Val Leu 245 250 255

Pro Glu Asp Leu Cys His Lys Phe Leu Gln Leu Ala Glu Ser Asn Thr 260 265 270

Val Arg Gly Ile Glu Thr Cys Gly Ile Leu Cys Gly Lys Leu Thr His 275 280 285

Asn Glu Phe Thr Ile Thr His Val Ile Val Pro Lys Gln Ser Ala Gly 290 295 300

Pro Asp Tyr Cys Asp Met Glu Asn Val Glu Glu Leu Phe Asn Val Gln 305 310 315 320

Asp Gln His Asp Leu Leu Thr Leu Gly Trp Ile His Thr His Pro Thr

325 335 330

Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His Cys Ser Tyr 340 345

Gln Leu Met Leu Pro Glu Ala Ile Ala Ile Val Cys Ser Pro Lys His 360

Lys Asp Thr Gly Ile Phe Arg Leu Thr Asn Ala Gly Met Leu Glu Val

Ser Ala Cys Lys Lys Gly Phe His Pro His Thr Lys Glu Pro Arg

Leu Phe Ser Ile Cys Lys His Val Leu Val Lys Asp Ile Lys Ile Ile 405 410

Val Leu Asp Leu Arg 420

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Pro Asp His Thr Asp Val Ser Leu Ser Pro Glu Glu Arq Val Arq Ala 20 25

Leu Ser Lys Leu Gly Cys Asn Ile Thr Ile Ser Glu Asp Ile Thr Pro 35 40

Arg Arg Tyr Phe Arg Ser Gly Val Glu Met Glu Arg Met Ala Ser Val

Tyr Leu Glu Glu Gly Asn Leu Glu Asn Ala Phe Val Leu Tyr Asn Lys

Phe Ile Thr Leu Phe Val Glu Lys Leu Pro Asn His Arg Asp Tyr Gln 85

Gln Cys Ala Val Pro Glu Lys Gln Asp Ile Met Lys Lys Leu Lys Glu 100 105

Ile Ala Phe Pro Arg Thr Asp Glu Leu Lys Asn Asp Leu Leu Lys Lys 115 120 125

Tyr Asn Val Glu Tyr Gln Glu Tyr Leu Gln Ser Lys Asn Lys Tyr Lys 130 135 140

Arg Lys Arg Ile Ala Gln Met Arg Gln Gln Gln Leu Glu Ser Glu Gln 165 170 175

Phe Leu Phe Phe Glu Asp Gln Leu Lys Lys Gln Glu Leu Ala Arg Gly
180 185 190

Gln Met Arg Ser Gln Gln Thr Ser Gly Leu Ser Glu Gln Ile Asp Gly 195 200 205

Ser Ala Leu Ser Cys Phe Ser Thr His Gln Asn Asn Ser Leu Leu Asn 210 215 220

Val Phe Ala Asp Gln Pro Asn Lys Ser Asp Ala Thr Asn Tyr Ala Ser 225 230 235 240

His Ser Pro Pro Val Asn Arg Ala Leu Thr Pro Ala Ala Thr Leu Ser 245 250 255

Ala Val Gln Asn Leu Val Val Glu Gly Leu Arg Cys Val Val Leu Pro 260 265 270

Glu Asp Leu Cys His Lys Phe Leu Gln Leu Ala Glu Ser Asn Thr Val 275 280 285

Arg Gly Ile Glu Thr Cys Gly Ile Leu Cys Gly Lys Leu Thr His Asn 290 295 300

Glu Phe Thr Ile Thr His Val Ile Val Pro Lys Gln Ser Ala Gly Pro 305 310 315 320

Asp Tyr Cys Asp Met Glu Asn Val Glu Glu Leu Phe Asn Val Gln Asp 325 330 335

Gln His Asp Leu Leu Thr Leu Gly Trp Ile His Thr His Pro Thr Gln 340 345 350

Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His Cys Ser Tyr Gln 360

Leu Met Leu Pro Glu Ala Ile Ala Ile Val Cys Ser Pro Lys His Lys

Asp Thr Gly Ile Phe Arg Leu Thr Asn Ala Gly Met Leu Glu Val Ser 385 390 395

Ala Cys Lys Lys Gly Phe His Pro His Thr Lys Glu Pro Arg Leu 405 410

Phe Ser Ile Gln Lys Phe Leu Ser Gly Ile Ile Ser Gly Thr Ala Leu 420 425

Glu Met Glu Pro Leu Lys Ile Gly Tyr Gly Pro Asn Gly Phe Pro Leu 435

Leu Gly Ile Ser Arg Ser Ser Ser Pro Ser Glu Gln Leu 450 455

<210> 7

<211> 424 <212> PRT

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<400> 7

Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Glu Asp Arg Val Arg

Ala Leu Ser Gln Leu Gly Ser Ala Val Glu Val Asn Glu Asp Ile Pro

Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser

Ile Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn

Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr

Lys Ser Ala Val Ile Pro Glu Lys Lys Asp Thr Val Lys Lys Leu Lys

Glu Ile Ala Phe Pro Lys Ala Glu Glu Leu Lys Ala Glu Leu Lys

Arg Tyr Thr Lys Glu Tyr Thr Glu Tyr Asn Glu Glu Lys Lys Glu 115 120 125

Ala Glu Glu Leu Ala Arg Asn Met Ala Ile Gln Glu Leu Glu Lys 130 135 140

Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Gln Gln Leu Glu Gln Glu 145 150 155

Gln Phe His Ala Phe Glu Glu Met Ile Arg Asn Gln Glu Leu Glu Lys 165 170 175

Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Leu 180 185 190

Gly Gly Pro Leu Val Pro Asp Leu Glu Lys Pro Ser Leu Asp Val Phe 195 200 205

Pro Thr Leu Thr Val Ser Ser Ile Gln Pro Ser Asp Cys His Thr Thr 210 215 220

Val Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly 225 230 235 240

Ala Leu Ser Asn Ser Glu Ser Ile Pro Thr Ile Asp Gly Leu Arg His 245 250 255

Val Val Pro Gly Arg Leu Cys Pro Gln Phe Leu Gln Leu Ala Ser 260 265 270

Ala Asn Thr Ala Arg Gly Val Glu Thr Cys Gly Ile Leu Cys Gly Lys 275 280 285

Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Lys Gln 290 295 300

Ser Ala Gly Ser Asp Tyr Cys Asn Thr Glu Asn Glu Glu Glu Leu Phe 305 310 315

Leu Ile Gln Asp Gln Gln Gly Leu Ile Thr Leu Gly Trp Ile His Thr 325 330 335

His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350 \hspace{1.5cm}$

Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Val Ala Ile Val Cys Ser 355 360 365

Pro Lys Phe Gln Glu Thr Gly Phe Phe Lys Leu Thr Asp His Gly Leu 370 375 380

Glu Glu Ile Ser Ser Cys Arg Gln Lys Gly Phe His Pro His Ser Lys 385 390 395 400

Asp Pro Pro Leu Phe Cys Ser Cys Ser His Val Thr Val Val Asp Arg $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$

Ala Val Thr Ile Thr Asp Leu Arg 420

<210> 8 <211> 58

<212> PRT

<213> Homo sapiens

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Val Gly Arg Leu Glu Asn Ala Ile Gly Trp Tyr His Ser His Pro Gly 1 $5101515151510151510151015101$

Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Met Leu Asn 20 25 30

Gln Gln Phe Gln Glu Pro Phe Val Ala Val Val Ile Asp Pro Thr Arg

Thr Ile Ser Ala Gly Lys Val Asn Leu Gly 50 55

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<211> 58

<212> PRT

<213> Drosophila melanogaster

<400> 9

Val Gly Arg Met Glu His Ala Val Gly Trp Tyr His Ser His Pro Gly 1 5 10 15

Tyr Gly Cys Trp Leu Ser Gly Ile Asn Val Ser Thr Gln Met Leu Asn 20 25 30

Gln Thr Tyr Gln Glu Pro Phe Val Ala Ile Val Val Asp Pro Val Arg 35 40 45

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Thr Val Ser Ala Gly Lys Val Cys Leu Gly
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Ala Gly Arg Leu Glu Asn Val Val Gly Trp Tyr His Ser His Pro Gly
Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Arg Leu Asn
           20
                               25
Gln Gln His Gln Glu Pro Phe Leu Ala Val Val Ile Asp Pro Thr Arg
                           40
Thr Val Ser Ala Gly Lys Val Glu Ile Gly
  50
                      55
<210> 11
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<213> Caenorhabditis elegans
<400> 11
Glu Gly Arg Lys Glu Lys Val Val Gly Trp Tyr His Ser His Pro Gly
             5
                                   10
Tyr Gly Cys Trp Leu Ser Gly Ile Asp Val Ser Thr Gln Thr Leu Asn
            20
                            25
Gln Lys Phe Gln Glu Pro Trp Val Ala Ile Val Ile Asp Pro Leu Arg
Thr Met Ser Ala Gly Lys Val Asp Ile Gly
    50
<210> 12
<211> 58
<212> PRT
<213> Archaeoglobus fulgidus
<400> 12
Leu Pro Ile Gly Met Lys Val Phe Gly Thr Val His Ser His Pro Ser
              5
                                   10
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Pro Ser Cys Arg Pro Ser Glu Glu Asp Leu Ser Leu Phe Thr Arg Phe 20 25 30

Gly Lys Tyr His Ile Ile Val Cys Tyr Pro Tyr Asp Glu Asn Ser Trp $35 \hspace{1cm} 40 \hspace{1cm} 45$

Lys Cys Tyr Asn Arg Lys Gly Glu Glu Val 50 55

<210> 13

<211> 58

<212> PRT

<213> Pyrococcus horikoshii

<400> 13

Met Pro His Asp Glu Ser Ile Lys Gly Thr Phe His Ser His Pro Ser 1 $$ 5 $$ 10 $$ 15

Pro Phe Pro Tyr Pro Ser Glu Gly Asp Leu Met Phe Phe Ser Lys Phe 20 25 30

Gly Gly Ile His Ile Ile Ala Ala Phe Pro Tyr Asp Glu Asp Ser Val\$35\$

Lys Ala Phe Asp Ser Glu Gly Arg Glu Val

<210> 14

<211> 58

<212> PRT

<213> Thermoplasma volcanium

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Lys Pro Ile Asp Phe Ser Leu Val Gly Ser Val His Ser His Pro Ser 1 5 10 15

Gly Ile Thr Lys Pro Ser Asp Glu Asp Leu Arg Met Phe Ser Leu Thr 20 25 30

Gly Lys Ile His Ile Ile Val Gly Tyr Pro Tyr Asn Leu Lys Asp Tyr 35 40 45

Ser Ala Tyr Asp Arg Ser Gly Asn Lys Val 50 55

<210> 15

<211> 58

<212> PR7

<213> Methanobacterium thermoautotrophicum

<400> 15

Leu Pro Pro Phe Thr Gly Ala Val Gly Ser Val His Ser His Pro Gly
1 10 15

Pro Val Asn Leu Pro Ser Ala Ala Asp Leu His Phe Phe Ser Lys Asn 20 25 30

Gly Leu Phe His Leu Ile Ile Ala His Pro Tyr Thr Met Glu Thr Val\$35\$ 40 45

Ala Ala Tyr Thr Arg Asn Gly Asp Pro Val 50 55

<210> 16

<211> 58

<212> PRT

<213> Aquifex aeolicus

<400> 16

Ile Ser Lys Gly Met Glu Ile Val Gly Val Tyr His Ser His Pro Asp 1 5 10 15

His Pro Asp Arg Pro Ser Gln Phe Asp Leu Gln Arg Ala Phe Pro Asp 20 25 30

Leu Ser Tyr Ile Ile Phe Ser Val Gln Lys Gly Lys Val Ala Ser Tyr 35 40 45

Arg Ser Trp Glu Leu Lys Gly Asp Lys Phe 50

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<211> 60

<212> PRT

<213> Mycobacterium tuberculosis

<400> 17

Glu Asp Ala Asp Glu Val Pro Val Val Ile Tyr His Ser His Thr Ala 1 5 10 15

Thr Glu Ala Tyr Pro Ser Arg Thr Asp Val Lys Leu Ala Thr Glu Pro 20 25 30

Asp Ala His Tyr Val Leu Val Ser Thr Arg Asp Pro His Arg His Glu

35 40 45

Leu Arg Ser Tyr Arg Ile Val Asp Gly Ala Val Thr 50 55 60

<210> 18

<211> 58

<212> PRT

<213> Escherichia coli

<400> 18

Ile Lys Ile Asn Ala Ser Ala Leu Ile Leu Ala His Asn His Pro Ser 1 5 10 15

Gly Cys Ala Glu Pro Ser Lys Ala Asp Lys Leu Ile Thr Glu Arg Ile 20 25 30

Ile Lys Ser Cys Gln Phe Met Asp Leu Arg Val Leu Asp His Ile Val 35 40 45

Ile Gly Arg Gly Glu Tyr Val Ser Phe Ala 50 55

<210> 19

<211> 57

<212> PRT

<213> Drosophila melanogaster

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Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His Ser His Pro Gly 1 $$ 5 $$ 10 $$ 15

Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr Gln Gln Ser Phe 20 25 30

Glu Ala Leu Ser Glu Arg Ala Val Val Val Val Asp Pro Ile Glu 35 40 45

Ser Val Lys Gly Lys Val Val Ile Asp 50 55

<210> 20

<211> 57

<212> PRT

<213> Homo sapiens

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Thr Gly Arg Pro Glu Met Val Val Gly Trp Tyr His Ser His Pro Gly

1 5 10 15

Phe Gly Cys Trp Leu Ser Gly Val Asp Ile Asn Thr Gln Gln Ser Phe

Glu Ala Leu Ser Glu Arg Ala Val Ala Val Val Val Asp Pro Ile Gln

25

Ser Val Lys Gly Lys Val Val Ile Asp 50 55

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Glu Gln Leu Gln Ser Arg Ala Val Ala Val Val Val Asp Pro Leu Gln 35 40 45

Ser Val Arg Gly Lys Val Val Ile Asp 50 55

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1 5 10 15

Phe Gly Cys Trp Leu Ser Ser Val Asp Val Asn Thr Gln Lys Ser Phe 20 25 30

Glu Gln Leu Asn Ser Arg Ala Val Ala Val Val Val Asp Pro Ile Gln 35 40 45

Ser Val Lys Gly Lys Val Val Ile Asp 50 55